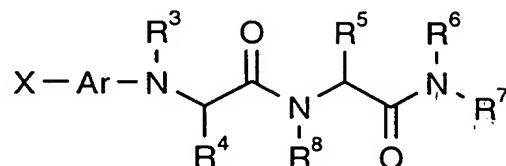


Claims

5 1. Compounds of the Formula



(I) wherein

X is $\text{H}_2\text{N}-\text{C}(=\text{NH})-$ or $\text{R}^1-\text{N}=\text{C}(-\text{NH}_2)-$, wherein

R^1 is $-\text{OH}$, $-\text{C}(=\text{O})\text{OR}^2$, alkyl, aralkyl, aralkyloxy or a heteroalkyl group, such as alkyloxy, acyl or acyloxy, wherein

R^2 is alkyl, heteroalkyl, carbocyclic, heterocycloalkyl, aryl, heteroaryl or aralkyl;

Ar is arylene, heteroarylene, or aralkylene wherein X is directly attached to the aromatic ring system;

R^3 is H, alkyl, heteroalkyl or aralkyl;

R^4 is H, an alkyl group which may be substituted with one or more $-\text{OH}$ or $-\text{NH}_2$ groups, a heteroalkyl group, a carbocyclic group, a heterocycloalkyl group, an aryl group, a heteroaryl group or an aralkyl group, which groups may be substituted with one or more groups selected from alkyl, heteroalkyl such as alkyloxy, acyl or acyloxy, a carbocyclic group, heterocycloalkyl, aryl, heteroaryl or aralkyl;

R^5 is H, alkyl, heteroalkyl, carbocyclic, heterocycloalkyl, aryl, heteroaryl or aralkyl;

R⁶ and R⁷ are independently H, alkyl, heteroalkyl, carbocyclic, heterocycloalkyl such as aryl-heterocycloalkyl, aryl, heteroaryl, aralkyl or heteroarylalkyl, which groups may be substituted with one or more groups selected from alkyl, heteroalkyl such as alkoxy, acyl or acyloxy, a carbocyclic group, heterocycloalkyl, aryl, heteroaryl, aralkyl, -OH or -NH₂, or are members of a heterocycloalkyl ring system, in particular an aryl-heterocycloalkyl ring system, or a heteroaryl ring system, which systems may be substituted with one or more groups selected from alkyl, heteroalkyl such as alkoxy, acyl or acyloxy, a carbocyclic group, heterocycloalkyl, aryl, heteroaryl, aralkyl, -OH or -NH₂; and

R⁸ is H, alkyl, heteroalkyl, carbocyclic, heterocycloalkyl, aryl, heteroaryl or aralkyl;

or a pharmacologically acceptable salt, solvate, hydrate or formulation thereof.

2. Compounds according to Claim 1, wherein

X is H₂N-C(=NH)- or R¹-N=C(-NH₂)-;

wherein R¹ is -OH or -C(=O)OR²;

wherein R² is alkyl, heteroalkyl, carbocyclic, heterocycloalkyl, aryl, heteroaryl or aralkyl;

Ar is arylene, heteroarylene, or aralkylene;

R³ is H, alkyl, heteroalkyl or aralkyl;

R⁴ is H, alkyl which may be substituted with -OH or -NH₂ groups, heteroalkyl, carbocyclic, carboxyalkyl ester, heterocycloalkyl, aryl which may be substituted with acyl groups, heteroaryl or aralkyl;

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R⁵ is H, alkyl, heteroalkyl, carbocyclic, or aralkyl;

R⁶ and R⁷ are independently H, alkyl, heteroalkyl, carbocyclic, heterocycloalkyl, aryl, heteroaryl, arylheterocycloalkyl which may be substituted with acyl groups, heteroalkylaryl which may be substituted with alkyl groups, aralkyl which may be substituted with acyl groups, or are members of the same heteroalkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl which may be substituted with alkylene groups, or aralkyl ring system, which may be substituted with -OH or -NH₂ groups; and

R⁸ is H;

or a pharmaceutically acceptable salt, solvate, hydrate or formulation thereof.

3. Compounds according to Claim 1 or 2, wherein
X is H₂N-C(=NH)- or HO-N=C(-NH₂)- or R²OC(=O)-N=C(-NH₂)-, R³ is H, Ar is meta-phenylene, and R⁵ is a small alkyl or an aralkyl group.

- Sub B2
4. Compounds according to Claims 1 to 3, wherein
X is H₂N-C(=NH)- or HO-N=C(-NH₂)- or R²OC(=O)-N=C(-NH₂)-, R³ is H, R⁴ is H, methyl, hydroxymethyl, isopropyl, 2-imidazolyl, 3-pyrazolyl, Ar is meta-phenylene, R⁵ is a small alkyl or an aralkyl group, and R⁸ is H.

5. Compounds according to Claims 1 to 4, wherein
X is H₂N-C(=NH)- or HO-N=C(-NH₂)- or R²OC(=O)-N=C(-NH₂)-, R³ is H, R⁴ is H, methyl, hydroxymethyl, 1,2-dihydroxyethyl, ethoxycarbonyl, isopropyl, cyclopropyl, 2-imidazolyl, 2-

pyrrolyl, 3-pyrazolyl, 2-pyridyl, 4-methoxycarbonyl-phenyl,

Ar is meta-phenylene,

R⁵ is a small alkyl or an aralkyl group,

R⁶ is H and R⁷ is optionally substituted 1H-indol-3-yl-ethyl, 4-hydroxy-phenylethyl, cyclohexyl, N-(2-methoxyphenyl)piperazinyl, 1,3-benzodioxol-5-ylmethyl, benzyl, phenethyl, 3,4-dimethoxyphenyl-1-ylmethyl, 2-methoxyphenyl-1-ylmethyl, 2-(4-morpholinyl)ethyl, 2-pyridinylethyl, 2-pyridinylpropyl, 3-pyridinylmethyl or R⁶ and R⁷ are part of a tetrahydroisoquinoline ring, a 4-thiomorpholine ring, a N-(2-methoxyphenyl)piperazine ring or a N-(4-methoxyphenyl)piperazine ring, and R⁸ is H

6. Compounds according to Claim 1, wherein

X is H₂N-C(=NH)- or HO-N=C(-NH₂)- or R²OC(=O)-N=C(-NH₂)-, R³ is H,

Ar is para-phenylmethylenegroup, and

R⁵ is a small alkyl or an aralkyl group.

7. Compounds according to Claims 1 and 6, wherein

X is H₂N-C(=NH)- or HO-N=C(-NH₂)- or R²OC(=O)-N=C(-NH₂)-, R³ is H,

R⁴ is H, methyl, hydroxymethyl, isopropyl, 2-imidazolyl, 3-pyrazolyl,

Ar is para-phenylmethylenegroup, and

R⁵ is a small alkyl or an aralkyl group.

8. Compounds according to Claims 1, 6 and 7, wherein

X is H₂N-C(=NH)- or HO-N=C(-NH₂)- or R²OC(=O)-N=C(-NH₂)-, R³ is H,

R⁴ is H, methyl, hydroxymethyl, 1,2-dihydroxyethyl, ethoxycarbonyl, isopropyl, cyclopropyl, 2-imidazolyl, 2-pyrrolyl, 3-pyrazolyl, 3- or 4-phenoxy-phenyl, 1,3-benzodioxol-5-yl, 2-pyridyl, 4-methoxycarbonyl-phenyl,

Ar is para-phenylmethylenegroup,

R⁵ is a small alkyl or an aralkyl group,

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R⁶ is H and R⁷ is optionally substituted 1H-indol-3-yl-ethyl, 4-hydroxy-phenethyl, cyclohexyl, N-(2-methoxyphenyl)piprazinyl, 1,3-benzodioxol-5-ylmethyl, benzyl, phenethyl, 3,4-dimethoxyphenyl-1-ylmethyl, 2-methoxyphenyl-1-ylmethyl, 2-(4-morpholinyl)ethyl, 2-pyridinylethyl, 2-pyridinylpropyl, 3-pyridinylmethyl or R⁶ and R⁷ are part of a tetrahydroisoquinoline ring, a 4-thiomorpholine ring, a N-(2-methoxyphenyl)piperazine ring or a N-(4-methoxyphenyl)piperazine ring, and R⁸ is H.

9. Pharmaceutical compositions containing a compound according to Claims 1 to 8 as the active agent and optionally carriers and/or adjuvants.

10. Pro-drugs, which are composed of a compound according to Claims 1 to 8 and at least one pharmacologically acceptable protective group which will be cleaved off under physiological conditions.

11. Process for the preparation of a compound according to Claims 1 to 8, wherein

a) a compound of Formula I, where X is a cyano group, is converted to a compound of Formula I, where X is a group of the Formula H₂N-C(=NH)- or R¹-N=C(-NH₂)-, and

b) this compound is optionally converted into a physiologically acceptable salt, solvate or hydrate.

12. Use of a compound, a pharmaceutical composition or a pro-drug according to claims 1 to 10 for the manufacture of medicaments for the inhibition of tryptase.

13. Use of a compound, a pharmaceutical composition or a pro-drug according to Claims 1 to 10 for the manufacture of medicaments for the treatment and/or prevention of diseases that are mediated by tryptase activity.

14. Use of a compound, a pharmaceutical composition or a

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pro-drug according to Claims 1 to 10 for the manufacture of medicaments for the treatment and/or prevention of allergic or inflammatory diseases.

- 5 15. Use of a compound, a pharmaceutical composition or a
pro-drug according to Claims 1 to 10 for the manufac-
ture of medicaments for the treatment and/or prevention
of asthma, allergic rhinitis, chronic obstructive pul-
monary diseases, emphysema, viral and bacterial pulmo-
10 nary infections and inflammatory responses, rheumatoid
arthritis, multiple sclerosis, osteoarthritis, dermatological
diseases, psoriasis, conjunctivitis, inflamma-
tory bowel diseases, peptic ulcers, cardiovascular dis-
eases, anaphylaxis and cancer.

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